MAGNOLIA MEDICAL TECHNOLOGIES

State of Sepsis Awareness 2023

Tammy Johnson, AVP, Clinical Strategy

Learning Objectives

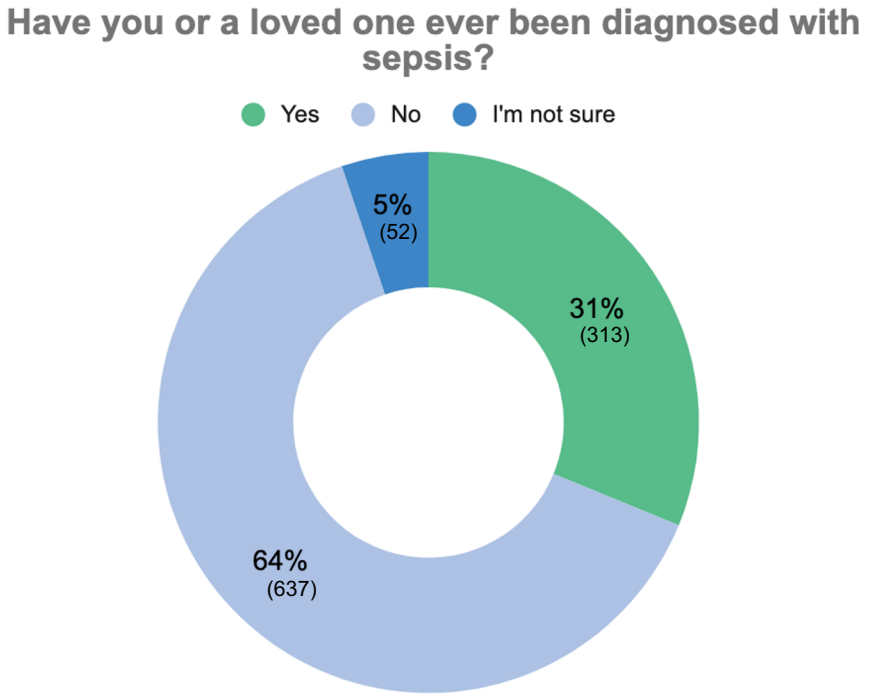
- Understand that sepsis is the leading cause of death, re-admissions, and costs for U.S. hospitals.

- Apply the data from a recent survey conducted with over 1,000 Americans in which sepsis was also identified as the #1 most feared infection risk.
  - Analyze the responses from a subset of survey participants, that have either been directly diagnosed with sepsis and/or have had a loved one impacted
  - Compare their attitude and perspective on different healthcare topics, including the prescribing of antibiotics and antimicrobial resistance

- Acquire some context on the impact of evidence-based techniques and technologies in improving sepsis testing accuracy.

SEPSIS DIAGNOSIS

Almost one-third of the respondents surveyed (31%) said they or their loved ones have been diagnosed with sepsis in the past.

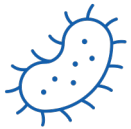


Note: N=1002, All Respondents.

Sepsis is the leading cause of death, readmissions, and costs in U.S. hospitals

According to 2017 data, globally, an estimated **49 million cases** of sepsis occur each year with **~11 million deaths (20% of all deaths)** reported. An estimated **1.7 million cases** of sepsis occur in the US annually with **approximately 350,000 hospital deaths or discharge to hospice.**

Sepsis is a leading cause of mortality and critical illness world-wide, with **hospital mortality rates of 25-30%**.
50% of survivors experience post sepsis syndrome and other effects including amputations.
Readmissions are 3 times more likely and 3 times more costly.



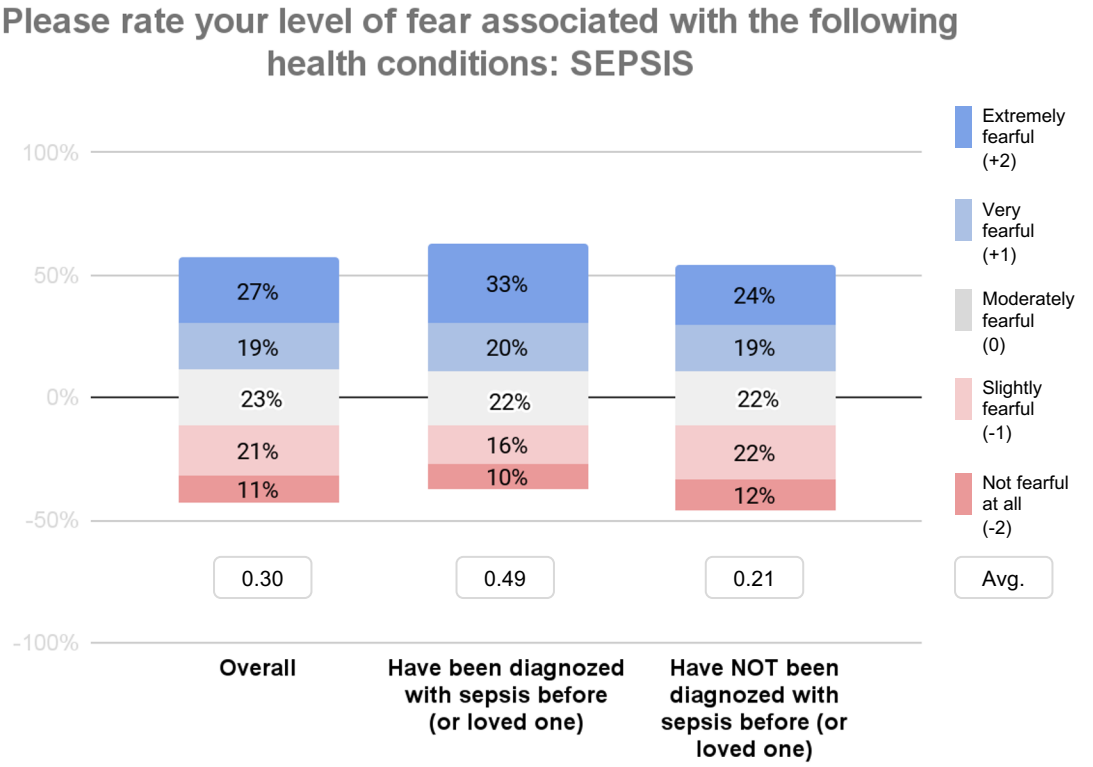
Clinical studies have demonstrated a **two-fold increase in mortality** caused by sepsis when **resistant organisms are the cause.**

Sepsis is the number one cost of hospitalization in the U.S. - more than **$24 billion** each year.

Liu V, Escobar GJ, Greene JD. Hospital deaths in patients with sepsis from 2 independent cohorts. JAMA. 2014;312(1):90-92. doi:10.1001/jama.2014.5804.
Weiss AJ, Jiang HJ. Overview of clinical conditions with frequent and costly hospital readmissions by payer, 2018. HCUP Statistical Brief #278. July 2021. Agency for Healthcare Research and Quality, Rockville, MD.
Dall C. WHO Say Sepsis Causes 20% of Global Deaths. CIDRAP. 2020.
Fleischmann C et al. Am J Respir Crit Care Med. 2016.
LaRosa SP. Sepsis. Cleveland Clinic Center for Continuing Education. 2010.
Sepsis Alliance Fact Sheet May 15, 2017.
Paquette K, et al. The FABLED Cohort Study. IDSA. 2021

FEAR OF SEPSIS

Respondents impacted by sepsis in the past had a 133% higher level of fear associated with sepsis, compared to those who have not been impacted by sepsis.

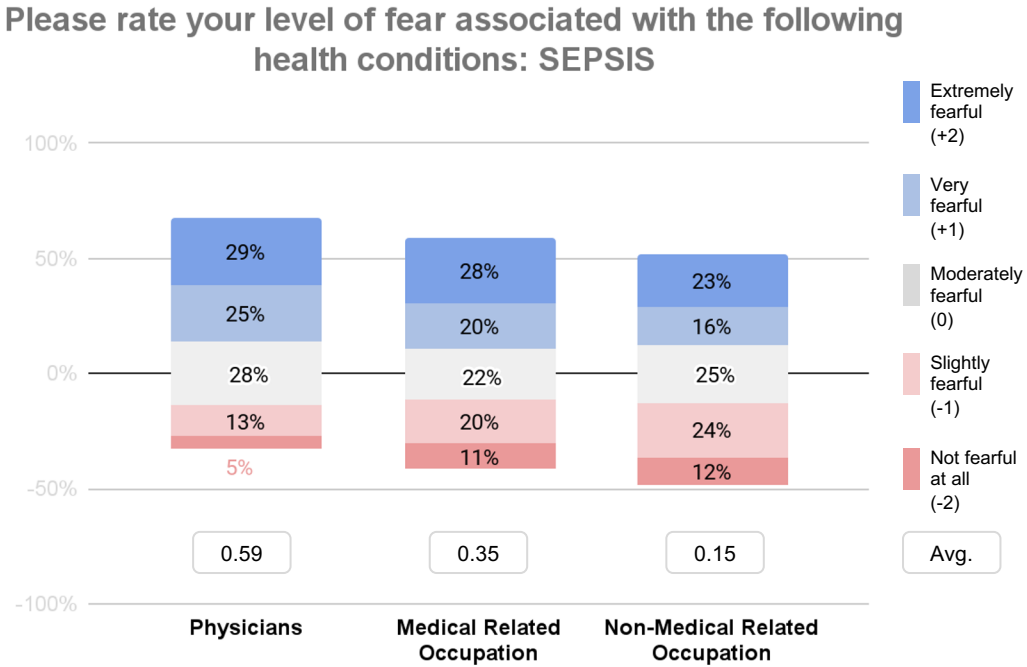


Note: not every survey respondent rated the level of fear, some of the respondents answered 'I don't know/Not applicable'. The sample size for respondents that rated the sepsis was 972. Averages were calculated by coding responses from a -2 to +2 to scale.

FEAR OF SEPSIS AND OCCUPATION

Respondents with a medical-related background also had a higher overall fear level of sepsis compared to those with a non-medical-related background.

Both segments (those directly impacted by sepsis and those with a medical-related occupation) most likely see first-hand the ravages of sepsis, which contributes to their higher fear level.



Note: not every survey respondent rated the level of fear, some of the respondents answered 'I don't know/Not applicable'. The sample size for respondents that rated the sepsis was 972. Averages were calculated by coding responses from a -2 to +2 to scale.

Sepsis a new definition:

Sepsis “A life threatening organ dysfunction caused by a dysregulated host immune response to infection”: **AND detailed report on its cause is fundamental**

National Institute of General Medical Sciences Sepsis

HHS Study: Journal of Critical Care Medicine, 2019

The Purpose of Blood Cultures

Confirm

the presence of microorganisms in the bloodstream

Identify

the microbial etiology of the bloodstream infection

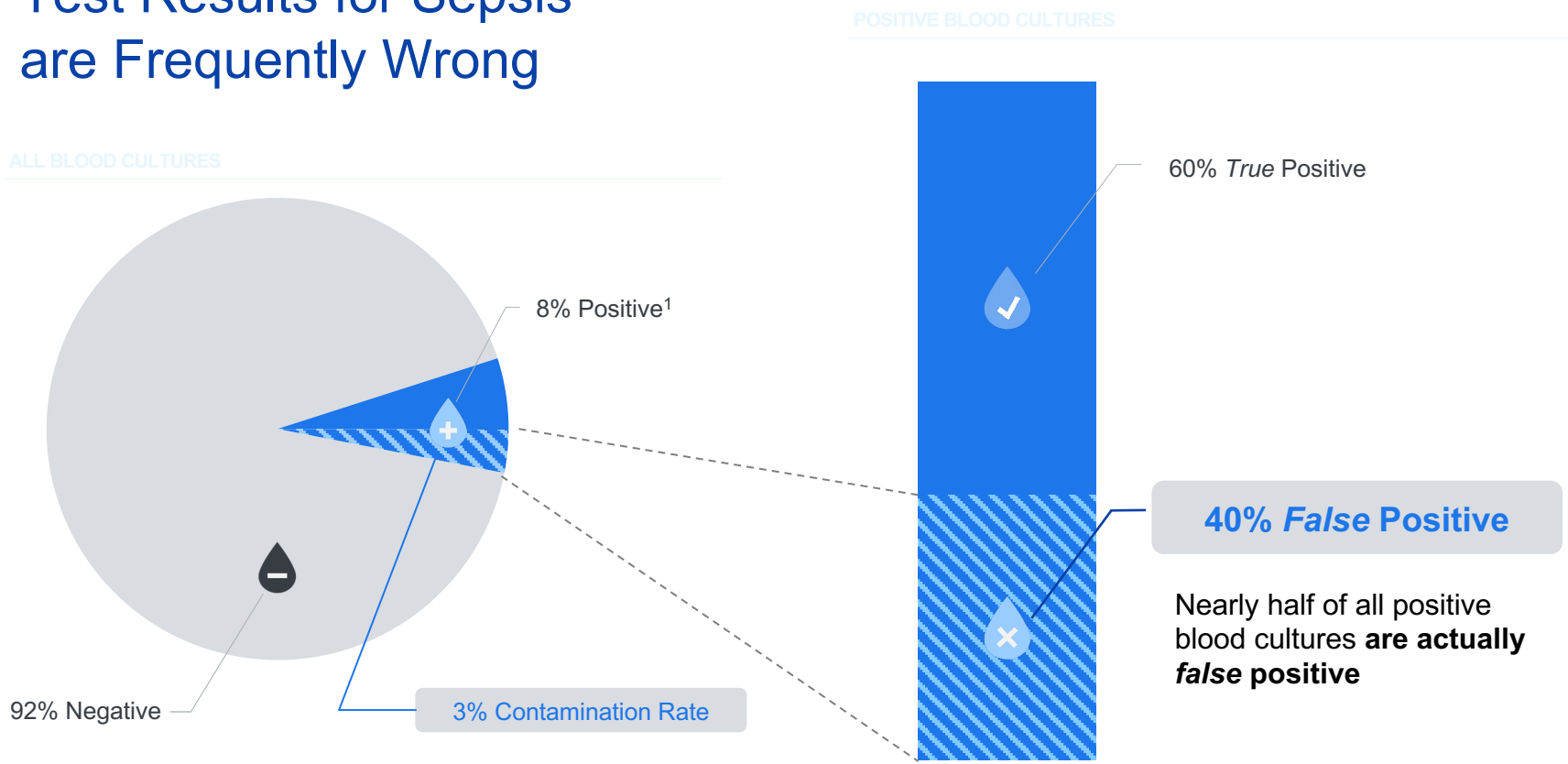
Help

determine the source of infection (e.g., endocarditis)

Provide

an organism for susceptibility testing and optimization of antimicrobial therapy

Test Results for Sepsis are Frequently Wrong



False positives are a **preventable error** and can lead to a misdiagnosis of sepsis

[1]Zwang O, Albert RK. Analysis of strategies to improve cost effectiveness of blood cultures. J Hosp Med. 2006;1(5):272-6. doi:10.1002/jhm.115.

Definition of a Blood Culture

- Blood culture contamination (BCC) is defined as the recovery of **normal skin flora (common commensal)** from a **single blood culture set when two sets are obtained**
- Culture is defined as a specimen of blood that is submitted for bacterial of fungal culture. **This is irrespective of the number of bottles or tubes into which the specimen is divided.**
- A BCC rate represents **common commensal organism occurrence in one set of blood cultures out of two sets obtained**
- **Blood Culture Set:** the combination of blood culture bottles or tubes **into which a single blood specimen is inoculated**
- **Required volume is essential and assumed**

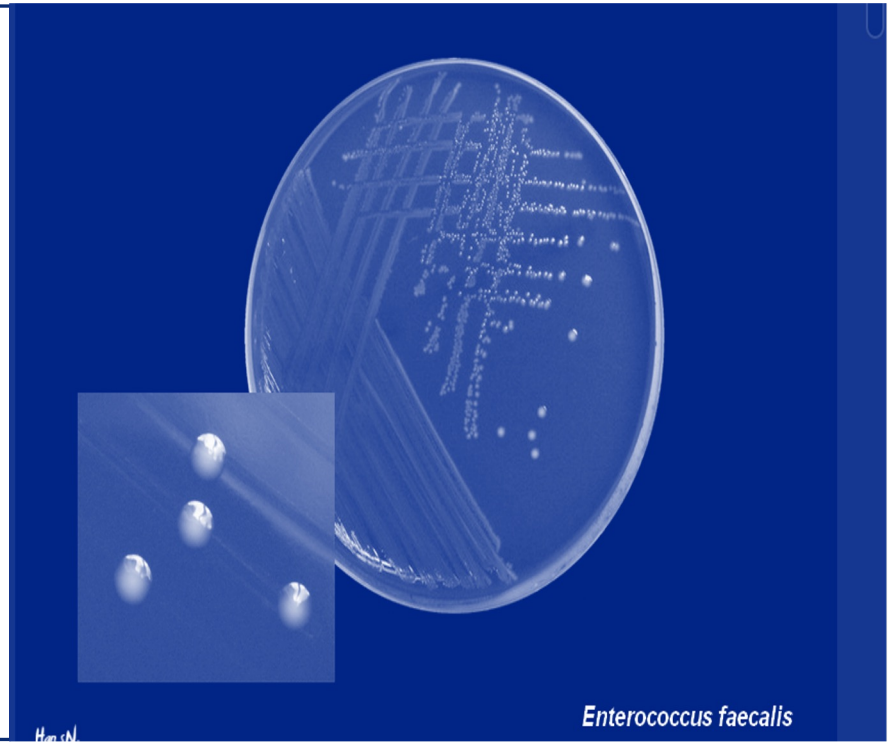
Hall and Lyman, CMR: Updated Review of Blood Culture Contamination; 2006
CLSI: M47A Principles and Procedures for Blood Cultures, Approved Guideline

Identity of the Organism

- Bates et al. found that the identity of the organism was the most important predictor for differentiating contaminated blood culture results from results indicating bacteremia
- **Common Commensal Organisms** or Probable Contaminants:
  - Coagulase-negative staphylococci (CoNS)
  - Propionibacterium spp. (Cutibacterium)
  - Aerococcus
  - Micrococcus
  - Bacillus spp. [not B. anthracis]
  - Corynebacterium spp. [diphtheroids]
  - Alpha-hemolytic streptococci

Identity of the Organism

- **Non-Common Commensal Organisms**
  (Usually a True Bacteremia or Fungemia)
  - Enterococcus
  - VRE
  - MRSA
  - Candida
  - E.coli
- Any organism NOT found on the NHSN Common Commensal list* is considered a recognized pathogen for NHSN reporting purposes



Common Commensal “Contaminators”

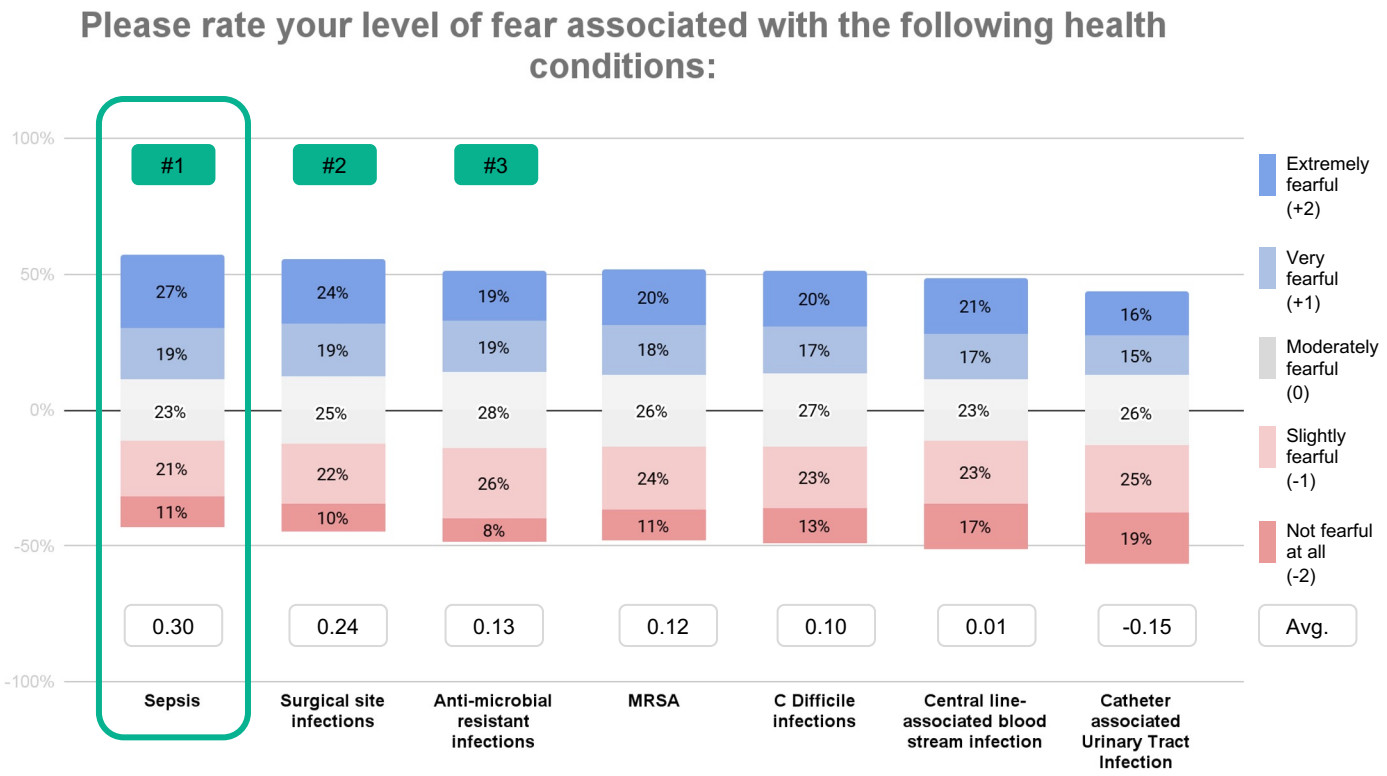
- Can be Pathogens
- Organisms can be difficult to interpret when isolated from blood cultures. One study showing:
  - Common Commensal Organisms
    - Clostridium perfringens were contaminants 77% (**27% were pathogens**)
    - Viridans group streptococci were contaminants 62% (**38% were pathogens**)

Pathogens can be contaminators but not defined as a blood culture contamination

  - Non-Common Commensal Organisms
    - Clostridium species were pathogens 80% (**20% were contaminants**)
    - Enterococci were pathogens 70% (**30% were contaminants**)

FEAR OF DIFFERENT INFECTIONS

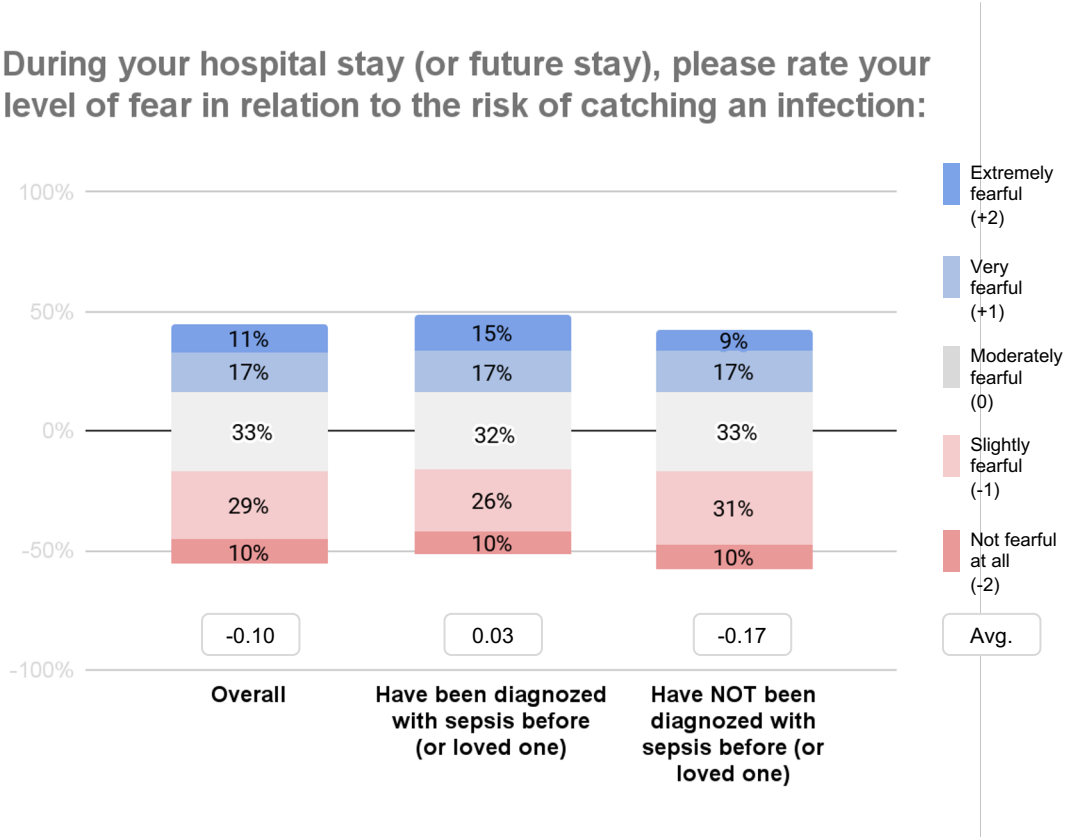
Sepsis was the most alarming infection fear for respondents with 46% indicating they are ‘Extremely’ or ‘Very’ fearful, followed by surgical site infections (43%), and AMR (38%).



Note: not every survey respondent rated the level of fear, some of the respondents answered ‘I don’t know/Not applicable’. The sample size for respondents that rated the sepsis was 972, surgical site infections - 980, bloodstream infections - 989, antimicrobial resistant infections - 987, MRSA - 952, C Difficile infections - 925, central line-associated bloodstream infection - 960, catheter associated urinary tract infection - 968. Averages were calculated by coding responses from a -2 to +2 to scale.

FEAR OF CATCHING AN INFECTION IN GENERAL

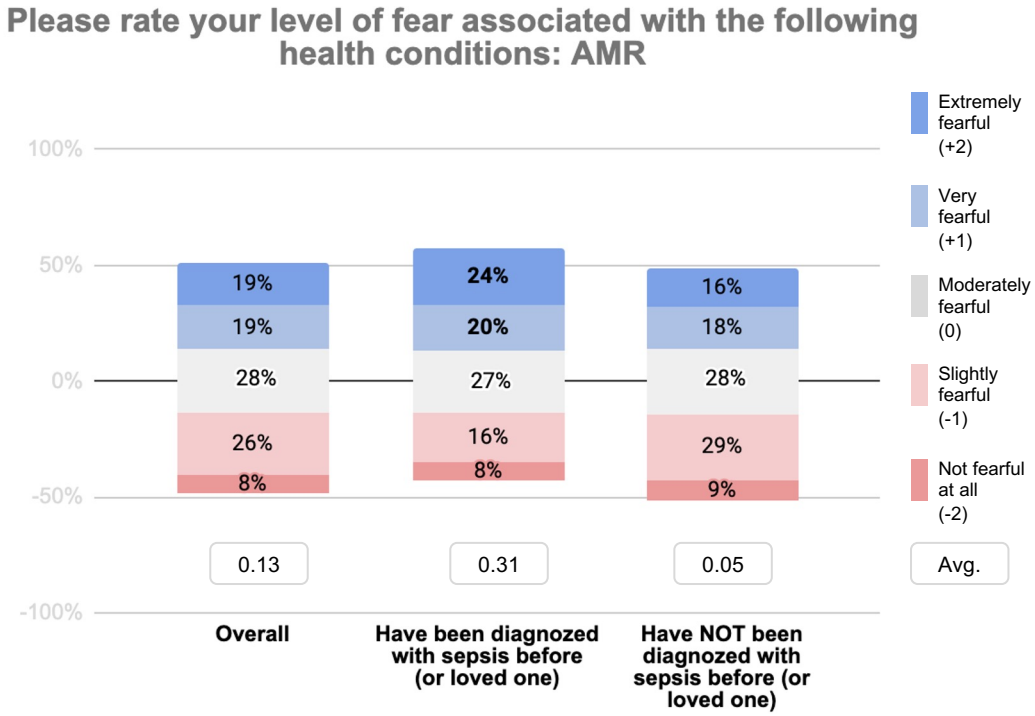
Respondents impacted by sepsis in the past were 67% more ‘Extremely fearful’ about catching an infection during the hospital stay compared to respondents without sepsis experience.



Note: N=1002, All respondents. Averages were calculated by coding responses from a -2 to +2 to scale.

FEAR OF AMR

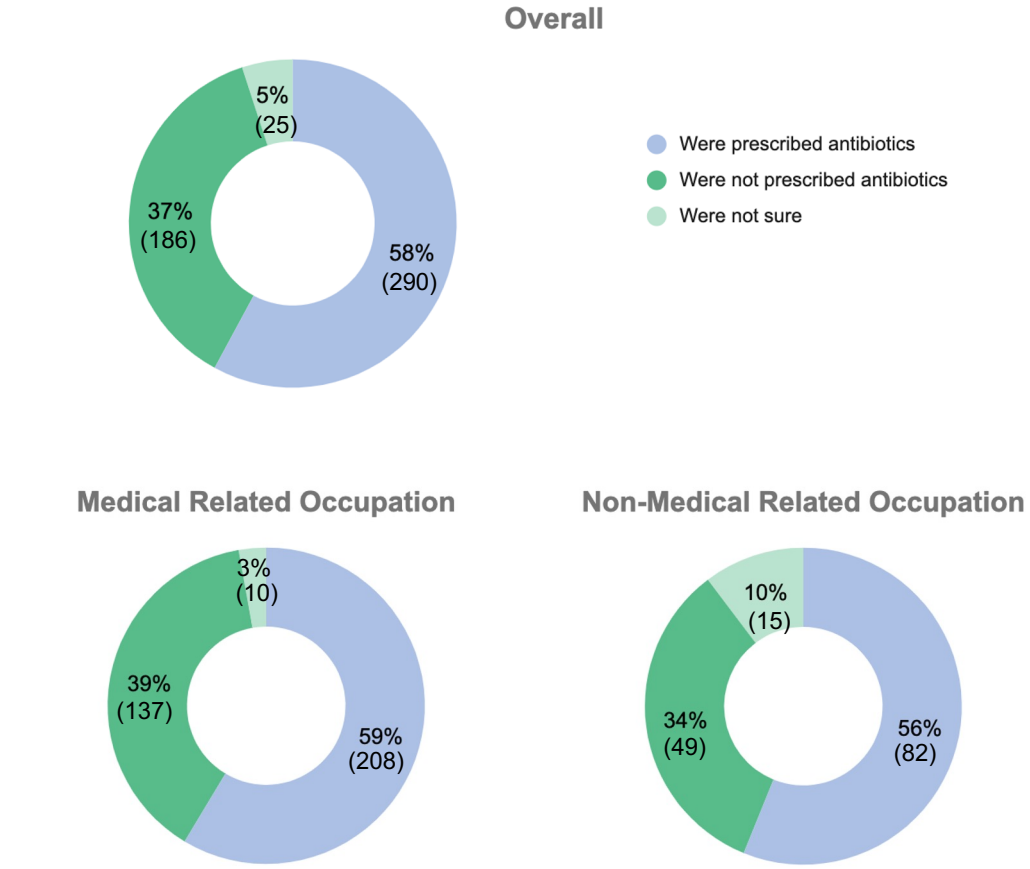
Respondents impacted by sepsis were also 520% more worried about AMR (antimicrobial resistance) compared to respondents without sepsis experience.



Note: not every survey respondent rated the level of fear, some of the respondents answered 'I don't know/Not applicable'. The sample size for respondents that rated the AMR was 987. Averages were calculated by coding responses from a -2 to +2 to scale.

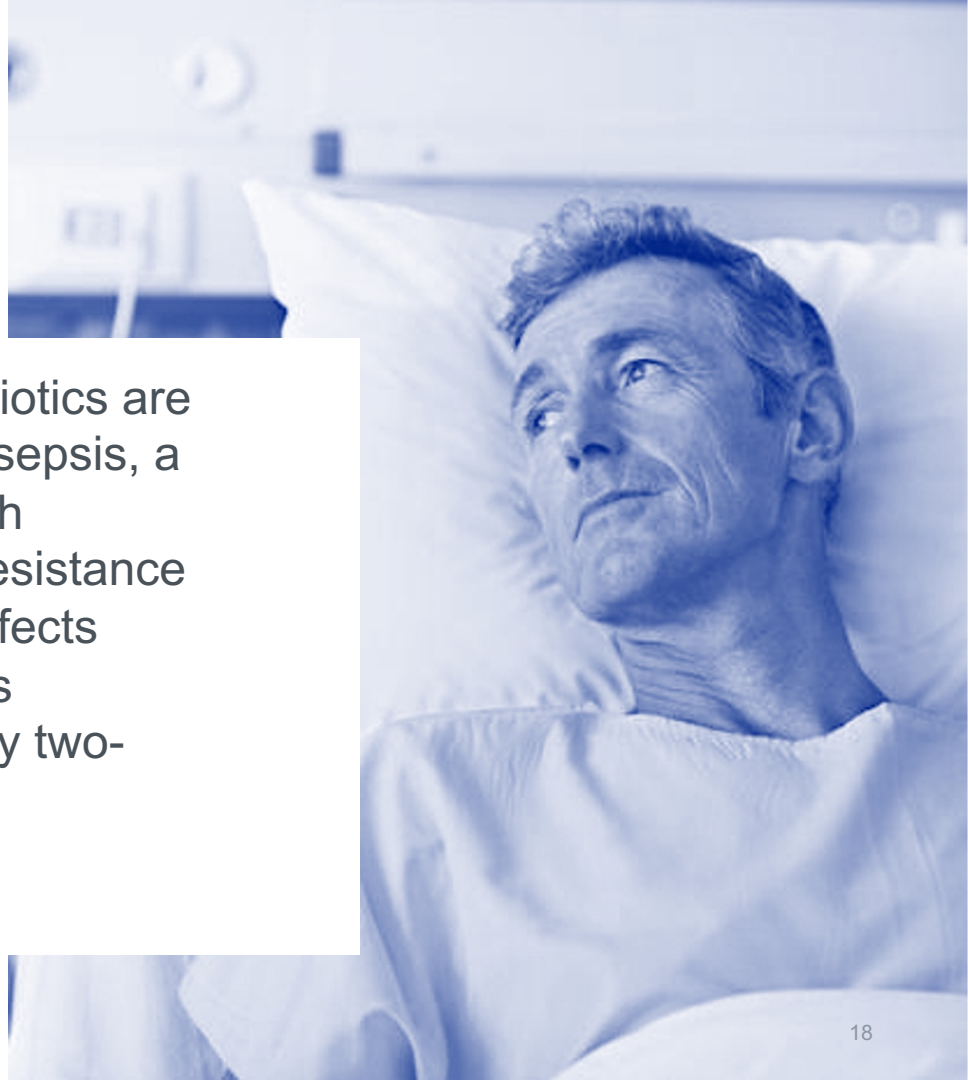
PRESCRIBING ANTIBIOTICS

Most respondents received antibiotic therapy during their hospitalization event.



Note: N=501, Patients and Caregivers.
Number of respondents for Medical and Non-Medical Related Occupation is shown in parentheses in the bottom charts.

Broad-spectrum Treatment



> “Although broad-spectrum antibiotics are integral in the management of sepsis, a major challenge associated with antibiotic therapy in sepsis is resistance by pathogens that adversely affects sepsis outcomes and increases mortality rates by approximately two-fold”

Pant, Amit, Journal of Biomedical Science, volume 28, article 6, 2021

The First Person in the World Saved by Antibiotics

- In March 1942, Mrs. Anne Miller of New Haven, Connecticut, was near death.*

Penicillin, Miracle Drug, Soon Out in Patent Forms; But Best See Doctor First

2019 AR Threats Report CDC

The Start of Resistance

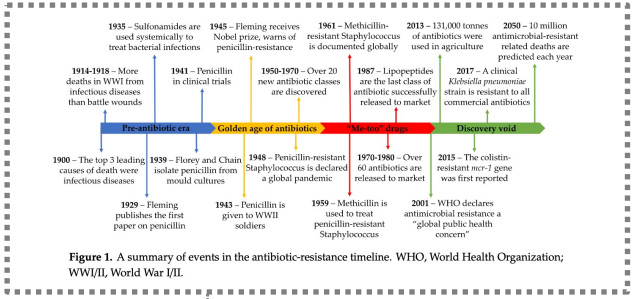


Figure 1. A summary of events in the antibiotic-resistance timeline. WHO, World Health Organization; WWI/II, World War I/II.

This pattern of resistance, first emerging in hospitals and then spreading to the community, is now a well-established pattern that recurs with each new wave of antimicrobial resistance

1942

Penicillin-resistant staphylococci were recognized, first in hospitals and subsequently in the community.

1944

94% of staph isolates were **susceptible** to penicillin by 1950 half were **resistant**

1945

Fleming received the Nobel prize and warned of antibiotic resistance, predicting that high public demand would create an era of abuse

1960

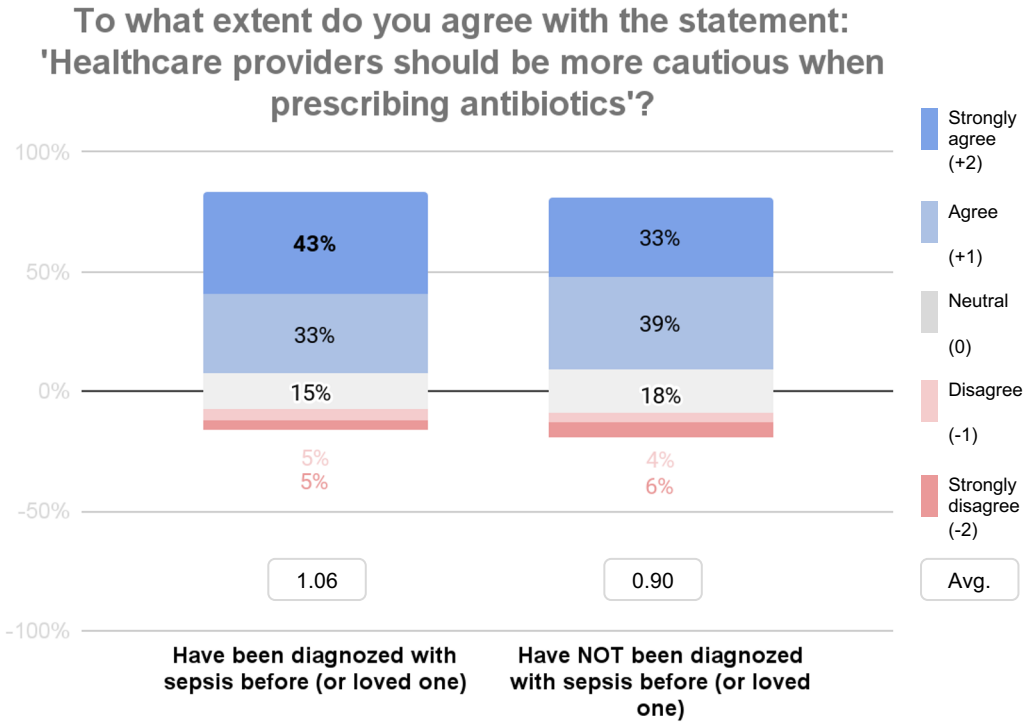
80% of both community- and hospital-acquired staphylococcal isolates were resistant to penicillin.

Lobanovska, Yale J Biol Med. 2017 Mar; 90(1): 135–145.Published online 2017 Mar 29
J Antimicrob Agents 2000 Nov16 Suppl 1:53-10; doi: 10.1016/s0924-8579(00)00299-5.Antibiotic resistance staphylococci
WHO A summary of events in the antibiotic-resistance timeline.

PRESCRIBING ANTIBIOTICS

Most respondents agreed that healthcare providers should be more cautious when prescribing antibiotics.

Those who had dealt with sepsis were 30% more likely to ‘Strongly agree’ that healthcare providers should be more cautious when prescribing antibiotics.

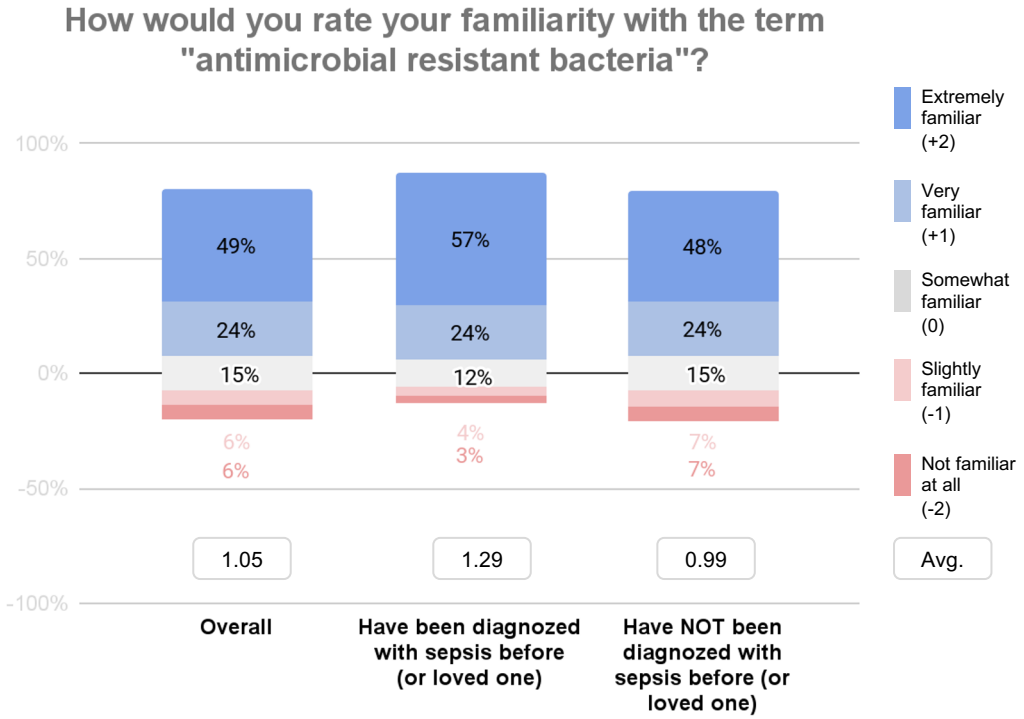


Note: N=1002, All Respondents.
Averages were calculated by coding responses from a -2 to +2 to scale.

FAMILIARITY WITH AMR

Most respondents were at least slightly familiar with the term “antimicrobial resistant bacteria” (AMR).

Those impacted by sepsis possessed a 30% higher familiarity with the term.



Note: N=1002, All Respondents.
Averages were calculated by coding responses from a -2 to +2 to scale.

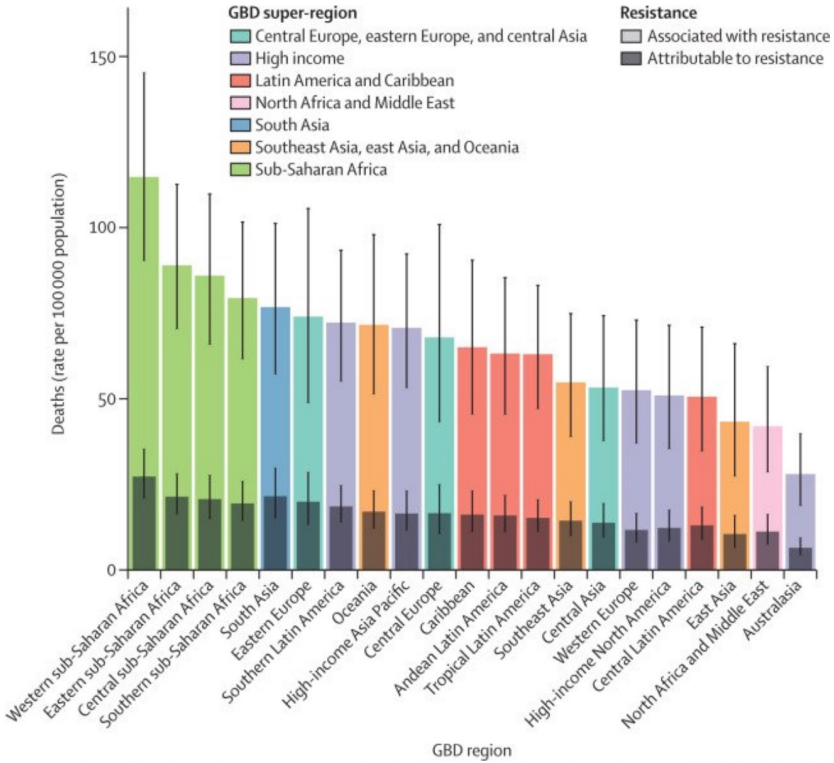
Global burden of bacterial AMR in 2019, a systematic analysis

- 4.95 million deaths associated with drug-resistant bacterial infections in 2019
- 1.27 million deaths directly caused by AMR

*"**By 2050, 10 million people will die from antibiotic resistant infections** if there are not changes…that will make antibiotic resistance the leading cause of death, ahead of cancer. This fundamentally challenges the very future of medicine. We know the problem is bad now, but the projections of what's going to happen if we don't do something are terrifying"*

Arjun Srinivasan, MD, Associate Director HAI Prevention
Division of Healthcare Quality Promotion, CDC

Murray, Global burden of bacterial AMR in 2019 a systematic analysis, The Lancet 2022



Rate of deaths attributable to and associated with bacterial antimicrobial resistance in 2019. (Antimicrobial Resistance Collaborators. The Lancet. 2022)

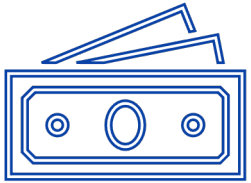
The Public Health Cost of Antibiotic Resistance

$20 Billion

for healthcare

$35 Billion

for loss of productivity



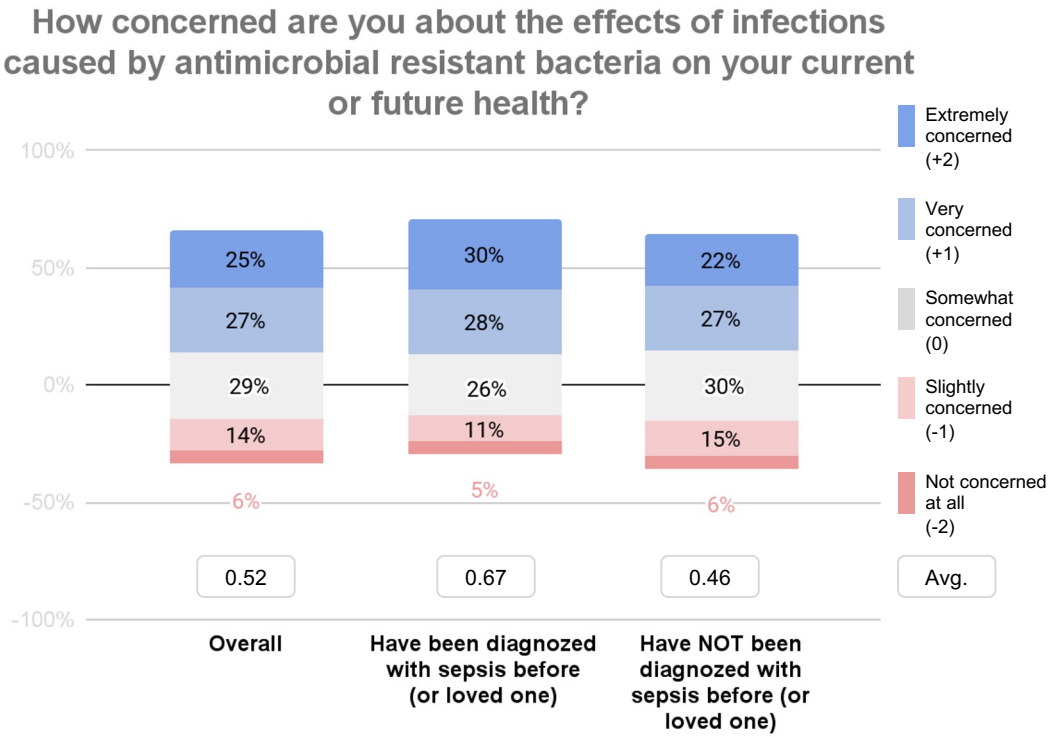
$55 Billion

in total annual costs

Porooshat Dadgostar, Journal of Infections and Drug Resistance: Antimicrobial Resistance: Implications and Costs. 2019 Dec 20. doi: 10.2147/IDR.S234610. PMCID: PMC6929930

EFFECTS OF INFECTIONS CAUSED BY AMR

Respondents who had sepsis in the past (or their loved ones) were also 46% more concerned “about the effects of infections caused by antimicrobial resistant bacteria on your current and or future health.”



Note: N=1002, All Respondents.
Averages were calculated by coding responses from a -2 to +2 to scale.

The Criticality of Antibiotics

- No new class of antibiotics has been developed since 1980's (Daptomycin)
- Antibiotic resistance and our high-risk patients critically dependent on antibiotics

Organ transplant

>33,000 organ transplants were completed in 2016/US

Chemotherapy

>650,000 people receive outpatient chemotherapy each year/US

Chronically ill

~30,000,000 with diabetes

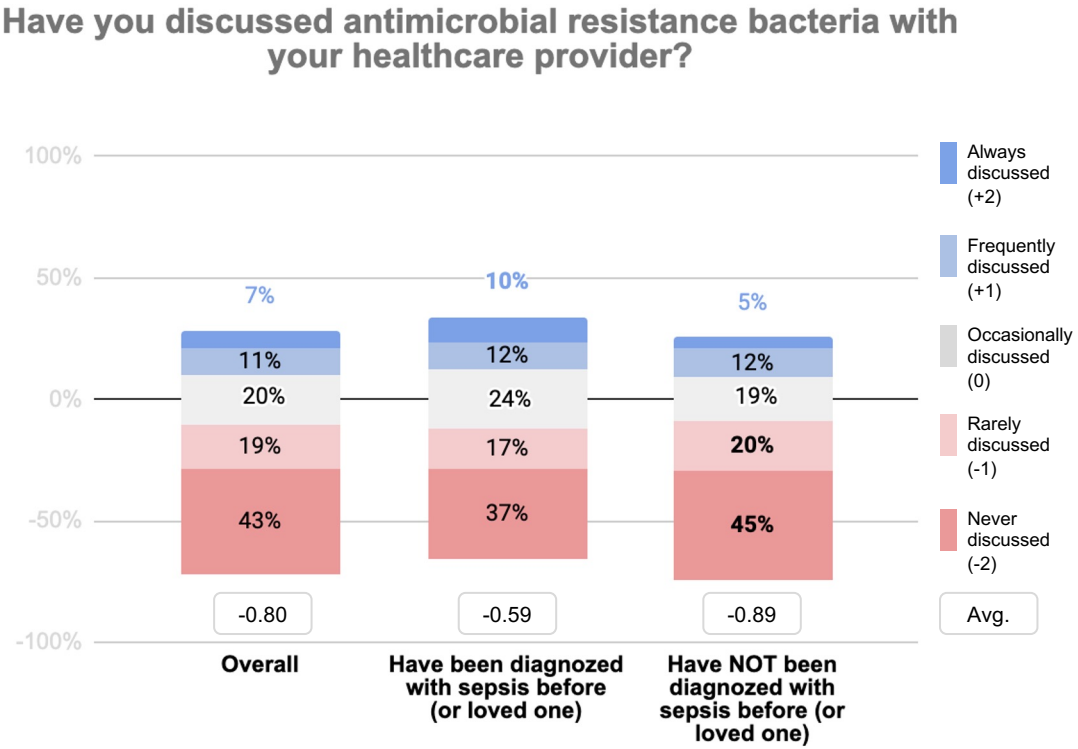
Renal patients

>500,000 received dialysis in 2016/US

Richard Baltz, Pewtrusts.org lead developer of Daptomycin
Llor, Carl Ther Adv Drug Saf 2013 Dec; 5(6):229-241
Milken Institute School of Public Health Antibiotic Resistance Action Network
2019 AR Threat Report CDC

DISCUSSING AMR WITH A HEALTHCARE PROVIDER

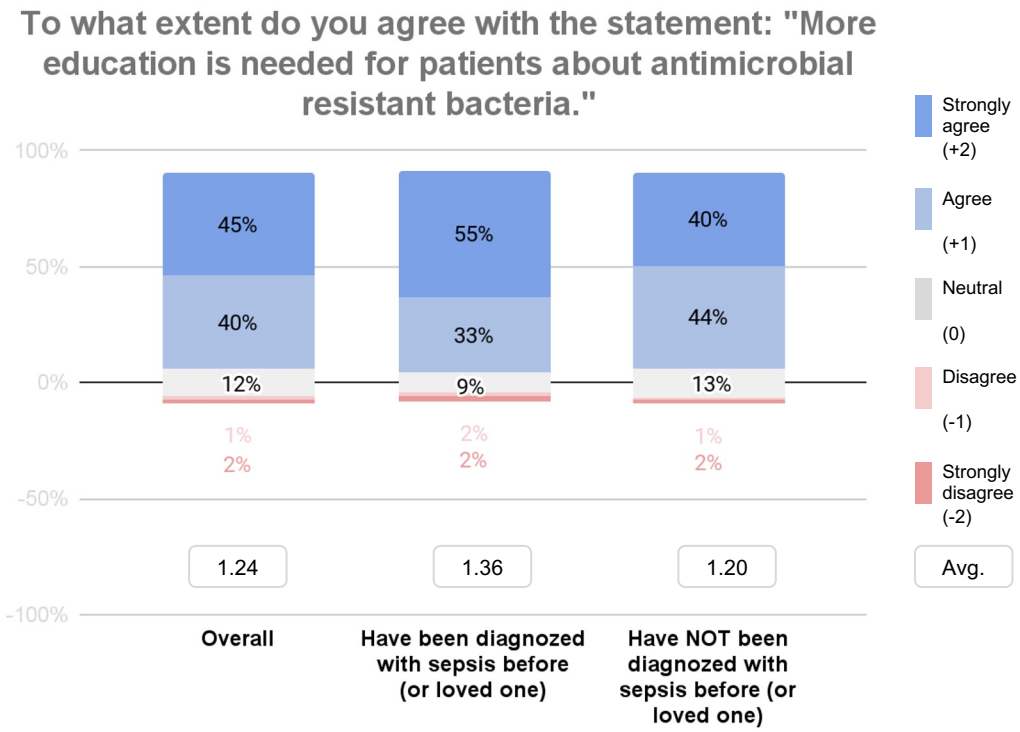
Respondents not impacted by sepsis, talked about AMR with their healthcare provider 34% less often than those who have been impacted by sepsis.



Note: not every survey respondent had a conversation with their healthcare provider, some of the respondents answered 'I haven't recently had a conversation with a healthcare provider'. The sample size for respondents that had a conversation was 903. Averages were calculated by coding responses from a -2 to +2 to scale.

EDUCATION ABOUT AMR

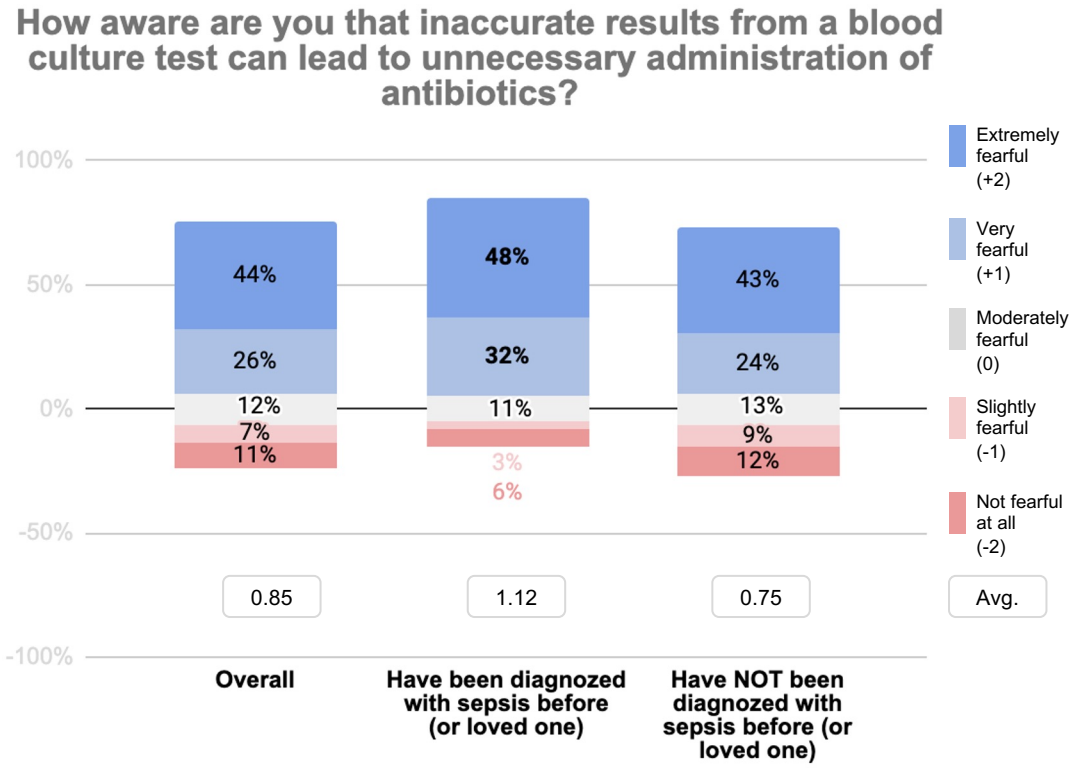
Respondents impacted by sepsis were 38% more likely to “Strongly agree” that “More education is needed for patients about antimicrobial resistant bacteria.”



Note: N=1002, All Respondents.
Averages were calculated by coding responses from a -2 to +2 to scale.

BLOOD CULTURE TESTS

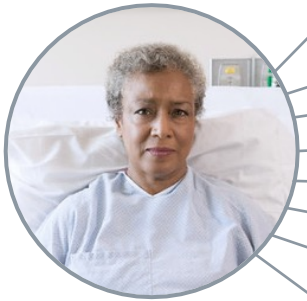
Respondents impacted by sepsis are 49% more aware “that inaccurate results from a blood culture test can lead to unnecessary administration of antibiotics” compared to those who have not been impacted by sepsis.



Note: N=1002, All Respondents.
Averages were calculated by coding responses from a -2 to +2 to scale.

False-positive blood cultures increase many harmful patient safety risks and mortality

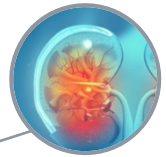
~40% of positive blood cultures are **False Positive**



Misdiagnosed Patient

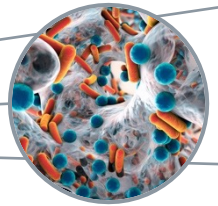
12-38% of the time, possible/probable contaminants **= true bacteremia**

Unnecessary Antibiotics
(up to 40% longer)

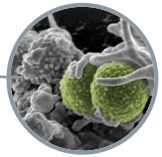


Acute Kidney Injury (AKI)
(as high as 36%)

Extended Length of Stay
(avg. 2.2 days)

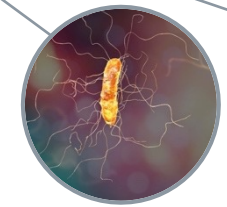


Antibiotic-Resistant Infections
(Incalculable)



Exposure to HAIs & HACs
(CDI, CLABSI, MRSA)

False-Positive CLABSIs
(30%-45%)



Risk of C. *difficile*
(30% reduction in broad-spectrum antibiotics could lower CDI by 26%)

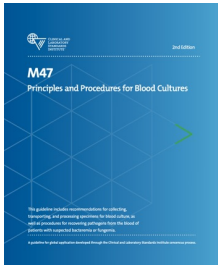
Increased Mortality
(up to 74%)

CDC 2019 AR Threat Report

“Diagnostics can be just as critical for fighting infections as antibiotics”

New National ‘Goal’

for blood culture contamination



CLSI M47 2022 and CDC’s new goal with best practices for blood culture contamination rates[1]

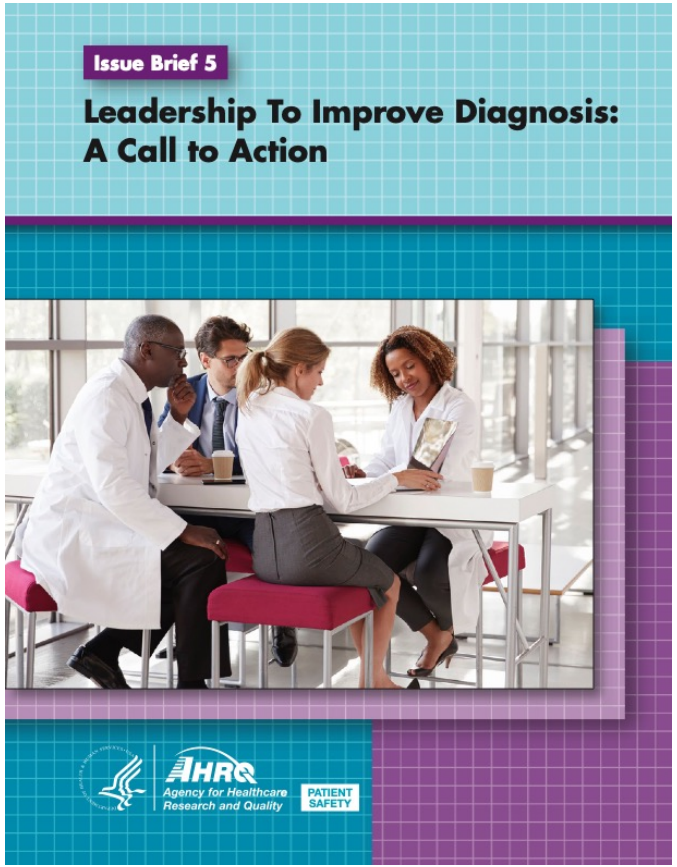
*All six cited studies examined the clinical efficacy of **Steripath** and/or referenced **Steripath-specific** datasets, and reported a sustained **1% or lower** contamination rate*

THE RIGHT ‘STANDARD’ FOR PATIENTS

[1]CLSI. M47 2nd Edition Principles and Procedures for Blood Cultures; 2022.

Agency for Healthcare Research and Quality

- AHRQ is the lead Federal agency investing in research to improve diagnostic safety and reduce diagnostic error.
- Improving Diagnostic Safety 2016 Diagnostic Safety Summit Information from AHRQ
- 2022 release of final report on “Diagnostic Error in the ED” This report lists sepsis as #6/7 out of the top 15 diagnostic errors in the ED.



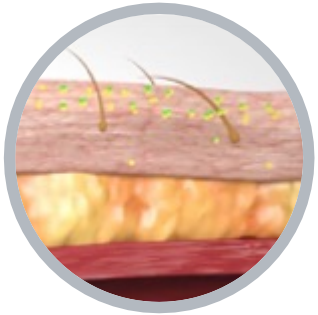
Murray, Global burden of bacterial AMR in 2019 a systematic analysis, The Lancet 2022

Training and Education on “Best Practices” Alone **Will Not** Solve the Problem

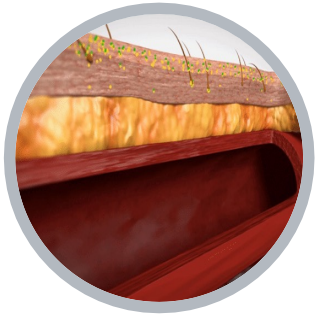
Controllable

Human Factor(s)
Risk of contamination during assembly, preparation of supplies and skin prep

Uncontrollable



Skin Flora
You can disinfect but not sterilize the skin. Up to 20% of skin flora remains viable in the keratin layer of the skin even after skin prep[1]



Skin Plug and Fragments
(uncontrollable factors)
will enter the culture specimen bottle and commonly will contain viable microorganisms (when present)

[1]Anjanappa T, Arjun A. Preparative skin preparation and surgical wound infection. J Evid Based Med. 2015;2(2):131-154. doi:https://doi.org/10.18410/jebmh/19. [2]Rupp ME, Cavalieri RJ, Marolf C, Lyden E. Reduction in blood culture contamination through use of Initial Specimen Diversion Device. Clin Infect Dis. 2017;65(2):201-205. doi:10.1093/cid/cix304. [3]Bell M, Bogar C, Plante J, Rasmussen K, Winters S. Effectiveness of a novel specimen collection system in reducing blood culture contamination rates. J Emerg Nurs. 2018;44(6):570-575. doi:10.1016/j.jen.2018.03.007.

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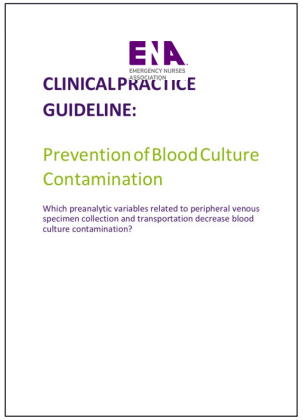
Patient Selection	Blood cultures should only be performed in patients with a reasonable likelihood of bacteremia/fungemia.
Skin disinfection *INS	Use a CHG and alcohol-containing disinfectant to scrub the phlebotomy site; adhere to recommended scrub and dry times
Blood Culture Bottle Top Disinfection *INS	Disinfect blood culture vial caps with alcohol for 15 seconds
Consideration	Leave an IPA or sterile pad on top of the BC bottle, to protect from environmental contaminants, until ready to inoculate with blood. IPA typically takes 5 seconds to dry
Phlebotomy Site *INS	Don't draw blood cultures through indwelling vascular catheters unless the catheter is thought to be the source of infection. In that case, remove NC and discard then draw from each lumen. Draw a second set from a peripheral venipuncture. Consider time to positivity. Send to lab within 2 hours, do not refrigerate sample
Sets *INS	Always draw two sets from different sites. Always draw blood cultures first and prior to antibiotics
Volume *INS	**I**s the single most important factor for organism detection. Draw volume per bottle IFU
Standardized Kits *INS	Use of standardized kits and procedures has proven helpful in preventing contamination
Phlebotomy Teams *INS	Educate and train individuals who perform blood cultures in aseptic technique
Surveillance and Feedback *INS	Monitor blood culture contamination and provide data to individuals and patient care units
Multidisciplinary Teams *INS	Sustained improvement in blood culture contamination is best achieved through a team approach.
Initial Specimen Diversion Device *INS	Divert and discard > 1mL of initial sample. Use of ISDD has been shown to decrease contamination rates to less than 1%.

Gorski LA, Hadaway L, Hagle ME, et al. Infusion therapy standards of practice, 8th edition. J Infus Nurs. 2021 Jan-Feb 01;44(1S Suppl 1): S1-S224.doi: 10.1097/NAN.0000000000000396 ENA Clinical Practice Guidelines
Doern GV, Carroll KC, Diekema DJ, et al. Practical guidance for clinical microbiology laboratories: a comprehensive update on the problem of blood culture contamination and a discussion of methods for addressing the problem. Clin Microbiol Rev. 2020;33(1):e00009-19. doi: 10.1128/CMR.00009-19.
Rupp ME, Cavalieri RJ, Marolf C, Lyden E. Reduction in blood culture contamination through use of Initial Specimen Diversion Device. Clin Infect Dis. 2017;65(2):201-205. doi:10.1093/cid/cix304.
Novak S, Dunne WM. Blood Culture: a key investigation for diagnosis of bloodstream infections. bioMerieux
CLSI. Principles and Procedures for Blood Cultures; Approved Guidelines. CLSI document M47-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2007.

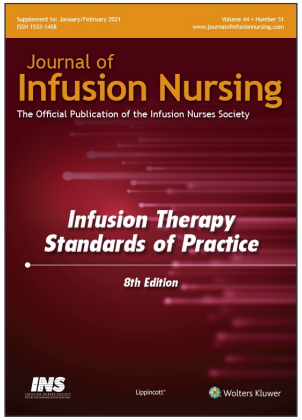
Evidence-Based Guidelines to Reduce Blood Culture Contamination

EMERGENCY NURSES ASSOCIATION



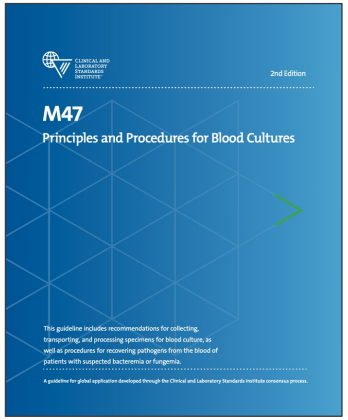
1.0–2.0 mL
diversion volume

INFUSION NURSES SOCIETY
SETTING THE STANDARD FOR INFUSION CARE®



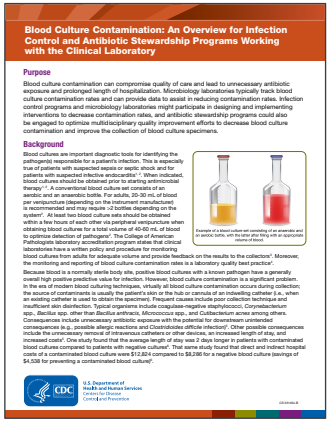
1.5 mL or greater
diversion volume

CLSI



1.0 mL
diversion volume
1% goal for blood culture contamination
(GP41 ED7 2017)
(M47 ED2 2022)

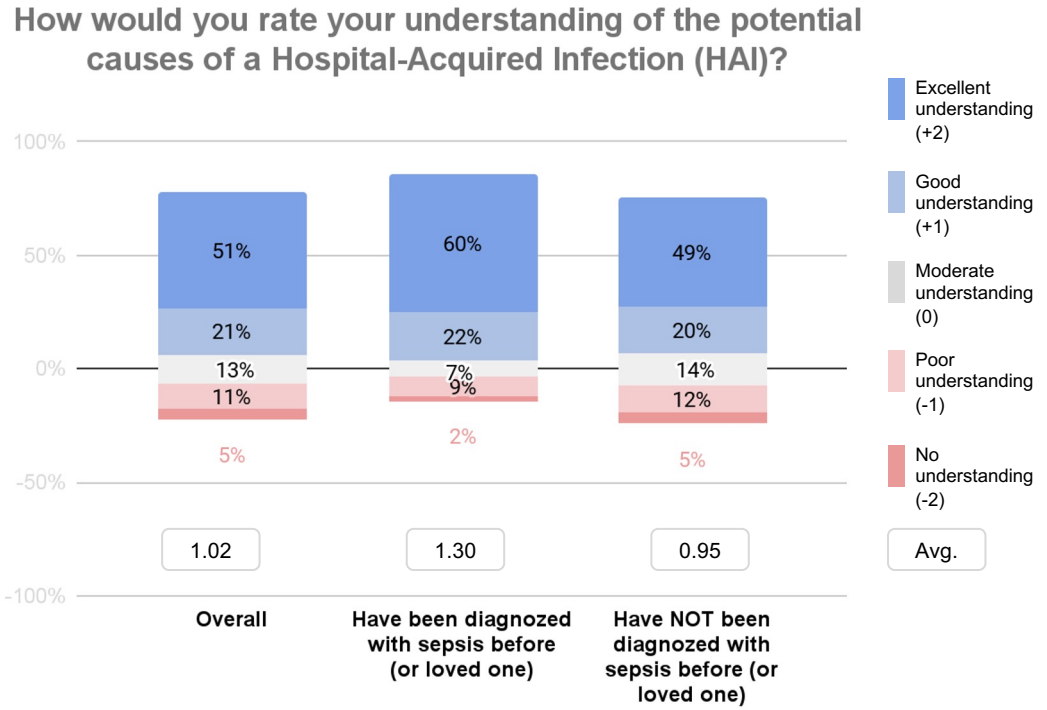
CDC



1% goal for blood culture contamination
(CDC Guidelines, 2022)

POTENTIAL CAUSES OF HAI

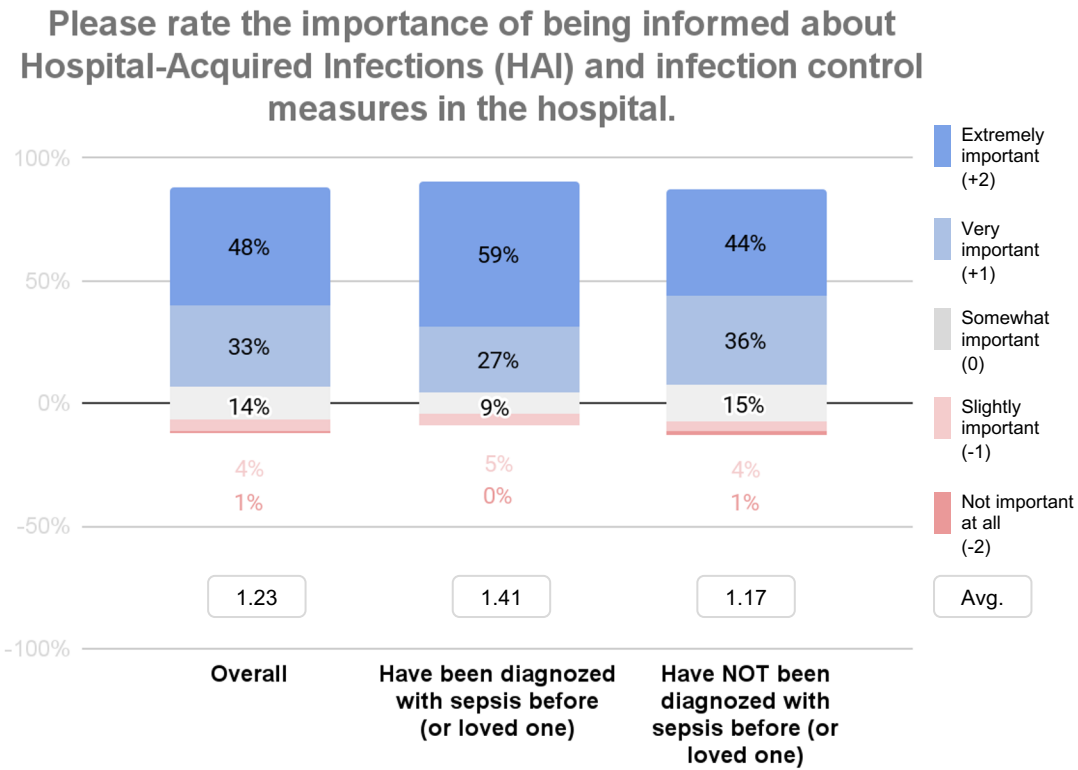
Respondents not directly impacted by sepsis have a 37% lower understanding of the potential causes of HAI versus those who have been impacted by sepsis.



Note: not every survey respondent rated the level of fear, some of the respondents answered 'I don't know/Not applicable'. The sample size for respondents that rated the sepsis was 972. Averages were calculated by coding responses from a -2 to +2 to scale.

IMPORTANCE OF BEING INFORMED ABOUT HAI

Respondents impacted by sepsis were 21% more likely to agree that it's important to be informed about HAI and infection control measures in the hospital versus those who have never been impacted by sepsis.



Note: not every survey respondent rated the level of fear, some of the respondents answered 'I don't know/Not applicable'. The sample size for respondents that rated the sepsis was 972. Averages were calculated by coding responses from a -2 to +2 to scale.

THANK YOU

“The names of the patients whose lives we save can never be known. Our contribution will be what did not happen to them. And, though they are unknown, we will know that mothers and fathers are at graduations and weddings they would have missed, and that grandchildren will know grandparents they might never have known, and holidays will be taken, and work completed, and books read, and symphonies heard, and gardens tended that, without our work, would never have been.”

Donald Berwick, MD, Founder of IHI